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EXHIBIT B



88-819

MM

4:00 Removed from CST to placement burr hole coil
 ^{31}P MRS shows ~~bottle~~ ~~lesion~~ - no injury

4:15 Normal T_{1W} anatomy
- apparently MCA was not occluded. Therefore, finding expected. Equally reduced signal intensity on T_{2W}.

4:45 Transcendal perfusion with 40 ml 2% TTC
Brain removed & immersed in 2% TTC for 5 min after
Initial impression is that MCA was not occluded.
No evidence of infarct on \odot cerebral hemispheres.
Brain stored in 10% buffered formalin.

Preliminary histological analysis shows mild cortical (ischemic) necrotic damage. No injury to subcortical structures, including basal ganglia, internal capsule. However, evidence of subarachnoid hemorrhage, periventricular

Colour slides

2.3 kg M.

11:00

30 mg/kg Nimbekal
intradermally I.V. femoral lines
MCAT surgery

11:28

1:40

MCAT-C (R) with considerable bleeding; packed with gauze
MAP 90-95 mmHg

 $\frac{1}{2}$ hour1:48 start T₂W (2800/80)

2:03 2:06 4.6 ml SO43 (1 mmol/kg) I.V.

CO2 14.0 AT T₂W I MAP 90 → 79 → 85 mmHg
2800/80 E₂U

OL 52 " 9~50 3/4
" " 5 min into sequence

2:15

B. DAT

" no apparent non-painful areas. " immediately following A

C. DAT

2:45 MAP 92 mmHg

" immediately following B

CO2 14.0 AT

2:53

" in prior to start

2:57 4.6 ml SO43 (1 mmol/kg) I.V. MAP 102 → 87 → 92 mmHg

2:58

E

immediately after D

3:00 MAP 97 mmHg

F

immediately after E

CO2 14.0 AT

T₁ 600/20



88-713 m

3.2 kg M.

PERMANENT MCA-0 : LACTATE MRI, SO43 INTC

11:30 30 mg/kg Nembutal
11:45 fentanyl internal i.v.
MCA surgery
12:58 MCA-0 (R) thermocanting + cut.

3:25 1W CSI C Hero core
MAP \approx 100 mmHg
3:30 0.3 ml Nembutal i.v. MAP 100 \rightarrow 90 mmHg
3:40 MAP 106 mmHg
3:50 T2W coronal multislice (TR/TE 2800/80, 100x100 FOV)
MM67A shows cortical hyperintensity in MCA territory w/ 4K
ipsilateral LV closure
4:15 MAP 105 mmHg
4:30 0.4 ml Nembutal
4:30 MAP 104 mmHg
5:15 MAP 113 mmHg
6:00 0.5 ml Nembutal MAP 115 \rightarrow 105 mmHg
 \rightarrow Complete report from Mike Mosley's record



C0221 + dat

88-892 m

Spectra
show lactate increase
& rise in P.

1/2 Dose

B. dat

pre-occ - pre-Py

New pictures

10 - N ✓
15 - O ✓
30 - P ✓
45 - Q ✓

C. dat - occ. + Py.

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

TAKE
2800/ice

4:15 - start regeneration
4:30 - injury Py

5:30

5:55

C. dat
1/2 dat - no contrast
1/1 dat

↓ change parameters
2800/ice

*L
OC-5
OC-50
OC-5
TC

spectra

2:00

2:20

3:40

4:00

4:55

001

002

003

004

005

pre-occlusion

post-occ

post-occ

post-occ

H-1

H-1

C-31

H-1

~~[REDACTED]~~ Occlusion/Reperfusion MCA Protocol : S043

2.8kg

Do
ROIS

11:05 30 mg/kg Nimboutal I.V.
 femoral vein + artery catheters
 MCA surgery

1:30 in CSI with suture line occluding snare performed
 around \textcircled{R} MCA; suture externalized in polyethylene tubing
 $\text{MAP} = 92 \text{ mmHg}$

C0221A.DAT $T_2 w/I$ to check coil interact.

2:00 $T_2 W$ coronal multisection shows partial \textcircled{R} LV closure + some nose ex.
 suggesting paral occlusion inadvertently.
 C0221.001 lactate 2:00 pre-ocu
 small lach 40/80

2:20 P-31 MRS shows Pi at 4.7 ppm (slightly acidic); otherwise norm
 ^1H MRS shows very small lactate
 w/ MRT, spectroscopy suggests partial constricted

.0W2 3P 2:30 pre-ocu
 1750 35

3:00 B.DAT $T_2 w/I$ 2000/80 w/utter in,
 S043 0.6mmol/kg = 2.8 ml MAP 95 \rightarrow 86 \rightarrow 94 mmHg.
 Start $T_2 W$ (2000/80) T2W with S043 shows slight perfusion defect (high signal)
 in BG ipsilateral; LV partly closed; slight generalized dilatation
 mass effect
 3:03 occlusion + in of O₂
 MCA-O \textcircled{R} + 0.6mmol/kg S043 over 4 min I.V. MAP 95 \rightarrow 85 \rightarrow 75
 C.DAT $T_2 w/I$ 2000/100 post con + post oce

CO221D.DAT T₂WI scanned after c
 CO221E.DAT T₂WI 2000/100
 scanned after D
 .003 spectrum 31P post-con
 .004 ¹H spectrum post-con
 4.00 μm F.DAT T₂WI 2000/100
 4.30 μm G.DAT T₂WI 2000/100
 post reper post con
 4.55 .005 31P spectrum post reper
 .006 ¹H spectrum post reper
 5.24 H.DAT T₂WI 2000/100
 post reper
 I.DAT T₂WI 2000/100
 post reper
 .007 evaluate RD spectrum 1Duls
 .008 " ECO8
 .009 short-TR

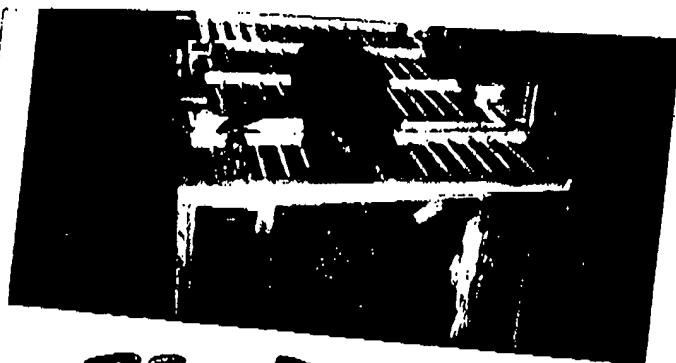
Start perfusion
 Large increase in lactate

T_2W collected from 3:04 - 3:16 (1-12 min post occlusion) shows high signal (perfusion defect) at BG but not cortical structures.

T_2W collected from 3:16 - 3:28 (13-28 min post occlusion) shows little signal difference. 12. plateau phase of SO4.

- 3:40 P-31 MRS shows slight Pi elevation
- 4:00 1H MRS shows lactate elevation in + D₂ 0.5 mmol/kg SO43 i.v. over 3 min
- 4:15 Start T_2W (2000/100) coronal multisection. Shows progressive perfusion defect in cortical area level forehead; BG also hyperintensity.
- 4:15 attempted reperfusion by releasing snare around MCA.
- 4:30 MAP 102 mmHg 0.5 mmol/kg SO43 i.v. Start T_2W coronal multisection (2000/100) Similar to post occlusion BG hyperintensity
- 5:05 P-31 MRS shows slightly elevated Pi at 4.7 ppm. - Similar to pre-occlusion, though oxygen improvement.
- 5:15 MAP 95 mmHg
- 5:30 T_2W (2000/100) coronal multisection shows mild cortical bright. Some mrs effect, pallidial; BG still
- 5:55 T_2W (2000/100) same as 5:30
- 6:05 Removed from CSZ
40 ml 20% TTE transcardially
Brain stored in 10% formalin
Dental impression is cortical infant

Note: proton spectra, lactate is evident, but overlapping fat is also present.



88-701 m

\downarrow possibly small amount of lactate

.003 'H post occ 1:22

.004 31P relatively normal spectra 1:28
B.DAT 2L50 q=40 2800/100

small decrease in PCr
rise in intensity in Pi region

3/4 1:40 post occ post con

\downarrow More lactate

.005 reperfusion 'H 2:00

.006 reperfusion 31P 2:07 \nearrow Back to pre-occ.
lactic

~~Something wrong~~ C.DAT

D.DAT

.007

.008

E

E24 31P

AOC1 9K 1500/80 MZ

H-1 323 EC08 1000/Tau128 Gv1500 60/120 50m/3

Tau192

E24 31P E24 2800/100 MZ Gv40 0.52

\downarrow Lactate evident .009

'H 4:15 after re-occ

.010 31P 4:25 ..

Evidence of injury again
decrease in PCr, rise

F.DAT

4:35 E24 2800/160 in a peak at
3.07 ppm

~~2.6 kg M~~ Occlusion/reperfusion MCA : SO43

9:45 30 mg/kg Nembutal I.V.
arterial + venous lines
MCA snare -
(R) MCA loosely ligated & cut, extralord in polyethylene tubing

12:00 Cat placed in CSZ
MAP 113 mmHg

CO2/CO

no lactate
evident

^1H spectrum pre-occlusion 12:40p-
0.02 ^3P pre-ox $\frac{\text{Normal}}{\text{spec}}$ 12:50
CO2/CO 0C 50 2800/100 3/4
an#0 1:05

1:15 MAP 115 mmHg

1:20 MCA - O (R) snare

1:35 MAP 116 mmHg MAP 117 \rightarrow 112 mmHg \rightarrow 117

^3P MRS shows no detectable lactate

1:40 1 mmol/kg deoxyguan DTPA I.V. at 4.77 ppm

1:42 2nd MCA reperfusion (5.2 ml) MAP stable

2:00 T2W coronal multislice shows signal hyperintensity lateral parietal cortex; otherwise, SO43 reduced signal T2W signal loss outside MCA territory "soft tissue edema" 0.4 ml Nembutal I.V.
Poor gray-white differentiation

2:05 MCA reperfusion

2:10 normal proton MRS

2:20 ^3P MRS shows lowered Pi - apparently successful reperfusion

2:25 1 mmol SO43 (5.2 ml) I.V.

2:30 MAP stable at 115 mmHg.

CO2/CO 2:30 Start T2W (2800/100)

2:47 T2W shows minimal SO43 induced changes in high signal intensity compared to reperfusion state
unclear whether reperfusion successful
poor gray-white contrast

6-045 2000/100 image 5:20 no con

3:10 diffuse image suggests normal perfusion
3:40 P-31 MRS suggests normal Pi / PCr.
MAP 120 mmHg

4:00 0.3 ml Nimbital i.v.

4:10 T2W coronal multisection suggests neuronal, if any, damage
surface parietal cortex. (D)

4:16 Re-occlusion MCA - Q (R)

4:25 P-31 MRS shows elevated Pi
4:40 1 mmol/kg SO43 i.v.
4:20 T2W (2000/100) coronal multisection
slightly higher signal intensity in cortical MCA territory
Generally appears similar to 1st postocclusion SO43 T2W
Poor grey/white contrast

5:30 T2W (2000/100) shows only slight ipsilateral mass effect +
cortical edema

6:15 Removed from CSF
perfused 1.5 hr with blue dye
Brain removed, shows absence of dye distal to MCA
occlusion site. However, may also reflect some degree
of hemorrhage induced by MCA transection just
before sacrifice.
Stained in 10% formalin overnight

[REDACTED] Colours slides

Some lactate
present in
baseline
spectra

slightly elevated Pi in baseline

CØ 307.001 H-1 - pre-occlusion

NT = 128
 $\bar{C} = 128$, PVA90 = 40 msec.

CØ 307.002 P-31 -

PVA90 = 35 msec.

NT = 236 pre-occlusion
2 sec. rep. time

- pretty normal

CØ 307B.dat

1st image after occlusion

$\text{TR/TE} = 2800/100$

OC - 50 GN - 20

2nd multislice after occlusion

$\text{TR/TE} = 2,000/100$

OC - 50
GN - 20

CØ 307.003
CØ 307.004

H-1
P-31

CØ 307D.dat

$\text{TR/TE} = 2800/100$

OC - 50

GN - 20

No. 2 slice

3/4

3:48
4:00

CØ 307.005
CØ 307.006

H-1
P-31

Occlusion/Reperfusion RCA

Kushangata (es2), N.K.
Sardis, W. China
CAT 88-849

1:00 Cat was hypoxic for ~ 3 minutes (He stopped breathing on the way down from Nakita's lab.)

1:05 Cat put on ventilator

1:20 Cat breathing on his own / placed in CSI

1:30 C0307.001 H-1 P-31 Pre-occlusion / RAP. 90

1:40 C0307.002 RAP. 90 Pre-occlusion / RAP. 90

2:00 C0307 A. dat T₂ TR/TE = 2800/80

2:10 RAP. 98 Pre-occlusion

2:24 120/98 RAP. 110 | Note (Baseline) ||

2:25 Start RCA Occlusion | some lactate
31P - normal |

2:28 start infusion D_yPTPA / started collecting

2:35 stopped infusion D_yPTPA of C0307C.001
RAP. 92 B

2:41 C0307C.001 TR/TE = 2,000/100

2:48 RAP. 94

3:00 C0307.003 H-1 → Lactate
3:15 C0307.004 P-31 Present
R_i slightly elevated

3:23 start reperfusion

infusion of D_yPTPA (not a full dose!)

3:35 ↑ RAP. 105 - 89 of 2.5 gds bolus

3:37 ↓

~~[REDACTED]~~ (cont.)

3:34 ~~S-18~~ CØ307D. dat - Post-~~repet.~~ repetition.
 3:43
 4:08 CØ 307. 005 H-1
 CØ 307. 006 P.31 repetition
 P. J. decrease
 4:35 CØ 307. 007 slightly
 4:45 CØ 307. 008 H-1
 P.31
 looks like full recovery
 5:30 CØ 307. 009 H-1
 5:40 CØ 307. 010 P.31
 6:00 CØ 307 E dat fine image
 (Backup on Sky/SN) TR/TE = 2800/100

Histology: MCA snare was inadvertently pulled while moving the animal from magnet. MCA was apparently transected. Subsequent TTC perfusion showed major hemispheric infarct probably unrelated to actual experimental lesion.

Brain stored in formalin.

~~[REDACTED]~~ Colour slides indicate total hemispheric infarct in MCA territory.

RSS8747e

1:04

Cat put in basket

1:35

H - 0031G.001

Do this
only

Third slice

4

5956.50
3370.37
4497.78
4735.12
4705.25

BIGC2

A	5838.37
B	3397.00
C	4369.25
D	4572.12
E	4531.00
A'	5893.75
B'	3341.50
C'	4385.37
D'	4629.12
E'	4908.62

1

5838.37
3397.00
4369.25
4572.12
4531.00

2

4558.00
3453.87
3585.62
3687.62
3649.62

3

6436.12
3786.50
4784.50
5023.25
5139.62

4

6027.5
3651.3
4526.12
4586.0
4614.5

3

6210.37
3337.00
4836.87
4930.5
4801.25

4

5935.0
4260.6
4873.1
4889.7
5014.5

Image #1

BIGC2

A	5305.37
B	3457.12
C	4233.62
D	4179.37
E	4537.37
A'	5689.62
B'	3370.62
C'	4480.50
D'	4530.50
E'	4532.50

1

5305.37
3457.12
4233.62
4179.37
4537.37

2

4752.87
3831.37
3976.50
3822.25
3840.12

3

604887
3601.12
4622.12
4485.75
4588.37

4

5841.75
3355.75
4555.25
4239.00
4575.5

3'

5925.87
4036.75
4971.37
5275.12
5446.50

4

5352.0
3872.02
4173.00
4253.50
4726.02

<u>Image #1</u>	MIC2	1	2	3	4
N	3784.12	3510.12	5100.5	4551.25	
O	2977.37	2845.5	3658.5	3417.37	
C	3662.75	3456.37	4900.5	4183.62	
Q	3811.37	3357.12	4794.6	4432.87	
R	3670.50	3228.62	5017.12	4305.75	
	1	2	3	4	
N	3729.25	3623.25	5084.25	5352.12	
O	2899.25	2774.62	3252.87	4708.25	
C	3669.75	3448.87	4556.25	5303.12	
Q	3733.75	3447.5	4993.5	5395.62	
R	3654.25	3381.62	4874.25	4806.87	

<u>Image #2</u>	MIC2	1	2	3	4
N	3580.25	3026.5	4609.62	41293.00	
O	2817.12	2757.87	2977.12	3055.12	
C	3386.25	2973.5	4351.00	405.02	
Q	3634.00	2921.62	4615.5	3982.62	
R	3768.12	2928.37	4207.00	3965.87	
	1	2	3	4	
N	3345.02	3050.75	4545.25	4314.75	
O	2689.87	2790.0	4062.75	4779.75	
C	3326.75	2961.87	4539.5	4406.25	
Q	3445.12	2982.75	4651.62	4600.12	
R	3273.57	2781.12	4358.5	4336.12	

<u>Image #3</u>	MIC2	1	2	3	4
N	4518.12	3620.25	5221.25	4641.12	
O	2941.02	3115.37	3187.87	3169.12	
C	4052.75	3522.37	4686.75	4228.37	
Q	4179.25	3610.37	5015.75	4477.8	
R	4003.75	3373.25	4797.5	3990.0	
	1	2	3	4	
N	4959.62	4423.50	5361.87	5124.75	
O	3182.87	3599.00	3110.02	5335.12	
C	4376.62	4153.00	4367.75	5547.75	
Q	4642.12	4204.87	4568.12	5301.75	
R	4596.00	4231.50	4883.25	5153.25	

Image #1

MR62		3920.87			
		1	2	3	4
N		4298.25	3227.62	482.87	4530.25
O		3146.25	3187.25	3217.62	3299.75
G		3925.75	2689.12	4019.00	4186.75
R		4282.12	3960.87	4272.12	4370.00
R		4012.37	3730.0	4309.12	4291.82
N		1	2	3	4
O		4506.62	4320.12	5071.5	4990.00
G		3528.6	3181.37	2850.12	4781.73
R		4327.25	4095.12	4389.37	5025.00
R		4370.00	4281.37	4757.62	4820.00
		4096.5	4120.37	4007.75	4454.75

MR62 ROI' Redone

✓	N	A
✓	O	B
✓	P	C
✓	Q	D
✓	R	E
✓	F	N
✓	U	O
✓	V	O
✓	W	O
✓	X	O

INS BS

Slice #3

2	White	3	SULCUS	4	NGC
---	-------	---	--------	---	-----

1' 2' 3' 4'

BIG62
T_{14c}
(min.) 0
15
30
45
75

N
N
N
Q
R
N
N
O
Q
Q

NBG
4483.0
2940.37
4023.75
4139.37
3994.6
INS BG
4915.3 ~~5001.12~~
4505.37 ~~4750.37~~
4750 ~~4607.5~~
5089.75
4859.12
\$870.00

BIG62
0 A
15 B
30 C
45 D
75 E

A
A
B
C
D
E

INS BG
\$870.00
4595.25
4825.25
4924.37
5111.62

7 3961.37
3514.37
N White
3550.37
3100.37
3468.12
3601.12
3294.37
INS White
3244.37
3514.37
3514.37
3792.12
3813.12
3805.75

N White
4574.5
3579.5
3605.8
3682.25
3614.00

5196.37
N Sulcus
5533.37
5388.62
5524.75
5514.12
5192.62
INS Sulcus
5533.37
5388.62
5524.75
5514.12
5192.62
INS

N Sulcus
4917.12
4526
35295.35
5349.62
5562.75
5574.25
5914.00
5924.25
5879.12
35335.77
5440.12
5537.62
5605.62

3092.37
3815.62
3905.58
3783.37
4030.87

INS Sulcus
5924.25
5879.12
35335.77
5440.12
5537.62
5605.62

1/2 half

C0221

0 B
15 C
30 D
45 E
60 F

0 B
15 C
30 D
45 E
60 F

NBG
3166.12
1892.87
2480.12
2727.37
2185.62

INS BG
3539.62
2221.87
2924.75
3201.75

N White
2768.25
2031.75
2439.62
2531.25
2866.5

INS

White
2229.37
1947.75
2240.37
2344.25

N Sulcus
2415.62
1631.75
2275.25
2408.32
2106.62

INS Sulcus
3821.37
1543.62
2102.62
2583.5

Sw. Sulcus

1344.75
2195.7
2211.5
2986.6
2405.25
2159.25
2405.37
1543.62
2102.62
2583.5

INS Grey
2867.62
2192.62
2064.62
2494.37

ROI's $\frac{1}{2}$ dose D₂/BG only
slice 4 CQ221*, fat

C CQ221 H4
15 N4 G
30 Q4 D
45 min. Q4 E

NBC
3324.57
~~1805~~ 1522
1805
1951

IBC
~~2504.12~~ 3049.25
2578
2465
2398.